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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,568	08/31/2000	Mary K. Danks	SJ-0011	7464

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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,568	DANKS ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,25 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,25 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/30/04 has been entered.

Claims 1-22, 24, 26, 30, and 31 have been canceled. Claims 23, 25, and 27-29 are still at issue and are present for examination.

Applicants' arguments filed on 1/30/04, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 23, 25, and 27-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claims as amended recite methods of using a rabbit carboxylesterase comprising SEQ ID NO:21. SEQ ID NO:21 is a protein sequence which includes the 18 amino acid leader peptide sequence. Use of the precarboxylesterase (i.e., the protein in which the signal sequence has not been removed) in the claimed methods is new matter. There is no evidence in the specification that applicants recombinantly produced **protein** includes the leader sequence. Pages 25-26 of the specification describe the features of the **DNA** which encodes the protein. Clearly the DNA encoding a secreted protein includes the sequence encoding the signal peptide as well as the sequence encoding the mature protein. The signal peptide is cleaved off following membrane translocation. There is no evidence in the specification that the recombinant protein produced actually retains this peptide. It is suggested that Claim 23 be amended to recite "a rabbit carboxylesterase recombinantly produced by expressing a polynucleotide encoding SEQ ID NO:21".

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 23, 25, and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Senter et al. (Reference AG of Applicant's PTO-1449) in view of Danks et al. (Reference AB of Applicant's PTO-1449) and Satoh et al. (Reference BA of Applicant's PTO-1449).

Senter et al. teach methods of increasing the activation of the prodrugs Paclitaxel and camptothecin (CPT-11) to active drugs in human and mouse tumor cells by the administration of rat serum carboxylesterase following administration of the prodrug.

Danks et al. teach that a recombinant rabbit liver carboxylesterase sensitizes human tumor cells to the prodrug

CPT-11. Footnote 4 of Danks et al. evidences that the rabbit liver carboxylesterase used by Danks et al. is that encoded by SEQ ID NO: 20. Danks et al. differs from the claimed invention only in that the methods of Danks et al. do not specifically include the administration of the rabbit liver enzyme to the tumor cells but instead the prior transformation of the tumor cells with a gene encoding the enzyme.

Satoh et al. describe the specific activity of a variety of mammalian carboxylesterases for the activation of CPT-11 to SN-38 (See Table 2) and show that rabbit liver carboxylesterases has one of the highest specific activities for this substrate and that the specific activity of the rabbit enzyme is four times greater than the specific activity of any of the rat enzymes.

Therefore it would have been obvious to one of ordinary skill in the art to use the recombinant rabbit enzyme of Danks in the methods of Senter et al. as Satoh et al. teach that the rabbit enzyme has a higher specific activity for the activation of the prodrug. While Senter does not do not teach the administration of the rat serum carboxylesterase prior to the administration of the prodrug as claimed in Claim 29, as Senter et al. suggest using the rat serum carboxylesterase for

cancer treatment and specifically state that "It may be possible to use rat serum carboxylesterase for prodrug activation *in vivo* by targeting the enzyme to tumors with an appropriate monoclonal antibody **and then** administering a prodrug such as PC or CPT-11" (emphasis added) they explicitly suggest the administration of the rat serum carboxylesterase prior to the administration of the prodrug. Furthermore, one of skill in the art would have been motivated to administer the carboxylesterase first in order for it to be targeted to the tumor prior to prodrug administration as this would minimize side effects due to activation of the prodrug in non-tumor cells.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Rebecca Prouty
Primary Examiner
Art Unit 1652